Vitamin C intake and susceptibility to pneumonia

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Feeding guinea pigs a diet deficient in vitamin C increases their susceptibility to infections, which may be caused by the effects of the vitamin on T lymphocytes and phagocytes (1). A few studies suggest that vitamin C intake affects human susceptibility to infections to some as yet unknown extent (1). In particular four trials involving British males showed an average 30% decrease in common cold incidence in groups given vitamin C, suggesting effects in certain population groups (2). Controlled trials have consistently found that large dose vitamin C supplementation alleviates the symptoms of the common cold, but the mechanism of this effect is poorly understood (1-3). Here we assess the relation of vitamin C intake to the incidence of pneumonia by analyzing findings from three controlled trials.

The literature on vitamin C and infectious diseases has already been explored thoroughly (1,2) and all controlled trials that reported the number of pneumonia cases in the study groups were selected for this analysis (Table 1). Fisher's exact test was used to calculate the one-tailed mid-P values (4) for each set of data separately. Exact hypothesis test for several 2×2 contingency tables (4) was used to calculate a one-tailed mid-P value for the combined data of two or three studies.

Three controlled trials have reported the number of pneumonia cases in a vitamin C group and a control group, each trial finding a considerably lower incidence of pneumonia in the group given vitamin C (Table 1).

Glazebrook and Thomson (5) studied schoolboys (15 to 20 years old) in an institution in the UK. No cases of pneumonia occurred in the vitamin C group. Placebo was not used, but because the vitamin was added to the food in the kitchen the placebo effect does not seem relevant. For practical reasons the subjects were not randomly allocated to the study groups, but certain administrative divisions were served vitamin-supplemented food and others remained as controls. A tonsillitis epidemic that affected all divisions uniformly the year before had shown that they could not be considered discrete units (5).

Kimbarowski and Mokrow (6) in the former Soviet Union investigated military recruits who had acquired influenza A infection. The number of pneumonia cases was significantly smaller in the vitamin C group. Placebo was not used and the allocation method was not described. Nevertheless the distribution of influenza severity was similar in both study groups.

Pitt and Costrini (7), primarily interested in whether vitamin C affects the common cold, carried out a randomized double blind placebo-controlled trial with military recruits in a training camp in the United States. Pneumonia incidence was substantially lower in the vitamin C group.

Each of these three trials found a ≥80% lower incidence of pneumonia in the vitamin C group. It is highly unlikely that the differences reported between the study groups in favor of the vitamin C groups would have occurred purely by chance ($P = 0.00002$). The study of Pitt and Costrini (7) is the most carefully conducted of the three, but the size of the effect is similar to the others. Thus there is no obvious tendency for the technically superior trial to show a smaller effect. If the Kimbarowski-Mokrow study is excluded from the analysis because it is technically the least satisfactory, there is still a highly significant difference in the pneumonia incidence between the vitamin C and control groups in the remaining two trials ($P = 0.0004$).

The notion that vitamin C intake may effect various infections is an old one (1,5,8,9). In 1917 Hess (10) concluded from his clinical experience with children that one of the important consequences of vitamin C deficiency was a markedly increased susceptibility to infection, pneumonia being a particular danger. In 1939 Sabin (11) reported about 5 cases of pneumonia in 25 rhesus monkeys deficient in

vitamin C whereas no cases were seen in 21 monkeys with adequate vitamin C intake (P = 0.02). The controlled trials assessed here suggest that vitamin C intake may affect susceptibility to pneumonia at least in some population groups.

A pertinent question as regards the interpretation of the three pneumonia trials is whether the differences between the study groups result mainly from a marginal deficiency in the control group or the high dose supplementation in the vitamin group. It was proposed previously that the reported decrease in common cold incidence in British males was better explained by a low dietary intake of vitamin C in the control group than by high dose supplements (2). Glazebrook and Thomson (5) estimated that their subjects obtained only 10 to 15 mg of vitamin C per day. Kimbarowski and Mokrow (6) did not explicitly estimate the dietary intake of their subjects but it seems likely that military recruits in the former Soviet Union also had a low intake. In both trials the vitamin dose administered was rather small, being in the range quite easily obtainable from diet (0.05 to 0.3 g/day). Accordingly the subjects of these two trials may have suffered from a marginal deficiency of vitamin C. Pitt and Costrini (7) did not estimate the dietary intake of their subjects but the whole blood vitamin C level was rather high initially (10 mg/l) and increased by only 36% when high vitamin C doses were administered (2 g/day), indicating the absence of marginal deficiency in the control group. Consequently the high dose supplementation seems to explain the difference between the study groups in this trial. In this respect these three trials do not invite a consistent and straightforward interpretation.

Because of the technical deficiencies in two trials (5,6) and the small number of pneumonia cases in each of the three trials, no firm conclusions can be drawn. Nevertheless the considerably lower pneumonia incidence in the vitamin C groups indicates that further work should be performed to address the question of whether vitamin C affects susceptibility to pneumonia more explicitly.

TABLE 1. Vitamin C supplementation and the incidence of pneumonia

Study *	Vitamin C dose (g/day)	Cases/Total		Difference in Incidence (%)	P (1-tail)
		Vitamin C group	Control group		
Glazebrook and Thomson (5), 1942	0.05-0.3	0/335	17/1100	-100	0.006
Kimbarowski and Mokrow (6), 1967	0.3	2/114	10/112	-80	0.009
Pitt and Costrini (7) 1979	2	1/331	7/343	-85	0.022

* Combined test for all three sets of data: P(1-tailed): 0.00002

References

1 Hemilä H. Vitamin C and infectious diseases. In: Packer L, Fuchs J, eds. Vitamin C in health and disease. New York: Dekker, 1997:471-503.

2 Hemilä H. Vitamin C intake and susceptibility to the common cold [see comments]. Br J Nutr 1997;77:59-72. Comments in: Br J Nutr 1997;78:857-66.
http://www.ncbi.nlm.nih.gov/pubmed/9059230
http://www.ltdk.helsinki.fi/users/hemila/H/HH_1997_BJN.pdf
http://dx.doi.org/10.1079/BJN19970201
http://www.ltdk.helsinki.fi/users/hemila/H/HH_1997_BJN2.pdf

3 Hemilä H. Vitamin C supplementation and common cold symptoms: problems with inaccurate reviews. Nutrition 1996;12:804-9.
http://www.ncbi.nlm.nih.gov/pubmed/8974108
http://dx.doi.org/10.1016/S0899-9007(96)00223-7
http://hdl.handle.net/10250/7979
http://www.ltdk.helsinki.fi/users/hemila/H/HH_1996_NUT.pdf

4 Rothman KJ. Modern Epidemiology. Boston: Little, Brown, 1986:161-2, 203-5.

5 Glazebrook AJ, Thomson S. The administration of vitamin C in a large institution and its effect on general health and resistance to infection. J Hyg 1942;42:1-19.
http://www.ltdk.helsinki.fi/users/hemila/CP/Glazebrook_1942_ch.pdf

6 Kimbarowski JA, Mokrow NJ. Farbige Ausfällungsreaktion des Harns nach Kimbarowski, als index der Wirkung von Ascorbinsäure bei Behandlung der Virusgrippe. Dtsch Gesundheitsw 1967;22:2413-8.
http://www.ncbi.nlm.nih.gov/pubmed/5614915
Translation at: thttp://www.ltdk.helsinki.fi/users/hemila/T4.pdf

7 Pitt HA, Costrini AM. Vitamin C prophylaxis in marine recruits. JAMA 1979;241:908-11.
http://dx.doi.org/10.1001/jama.241.9.908

8 Robertson EC. The vitamins and resistance to infection: vitamin C. Medicine 1934;13:190-206.
http://www.ltdk.helsinki.fi/users/hemila/CP/Robertsson_1934_ch.pdf

9 Perla D, Marmorston J. Role of vitamin C in resistance. Arch Pathol 1937;23:543-75, 683-712.
http://www.ltdk.helsinki.fi/users/hemila/animals/Perla_M_1937_1.pdf
http://www.ltdk.helsinki.fi/users/hemila/animals/Perla_M_1937_2.pdf

10 Hess AF. Infantile scurvy. Am J Dis Child 1917;14:337-53.

11 Sabin AB. Vitamin C in relation to experimental poliomyelitis with incidental observations on certain manifestations in *Macacus rhesus* monkeys on a scorbutic diet. J Exp Med 1939;69:507-15.
http://jem.rupress.org/cgi/content/abstract/69/4/507